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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,290	02/16/2006	Joseph Pandolfino	045952-0120	3390

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FOLEY AND LARDNER LLP  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER
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FELTON, MICHAEL J

ART UNIT	PAPER NUMBER
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1747

MAIL DATE	DELIVERY MODE
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01/19/2011

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/568,290	<b>Applicant(s)</b> PANDOLFINO, JOSEPH	
	<b>Examiner</b> MICHAEL J. FELTON	<b>Art Unit</b> 1747	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 184-201 is/are pending in the application.
- 4a) Of the above claim(s) 187-201 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 184-186 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Response to Arguments*

1. Applicant's arguments filed 11/19/2010 have been fully considered but they are not persuasive.

2. The applicant argues that, "Timko does not disclose tobacco plants with increased nicotine", (Remarks, 11/19/2010, page 9, paragraph 3). This is incorrect.

Timko et al. state,

It is also an object of the present invention to provide plant promoter regions that are capable of conferring high levels of transcription in rapidly dividing cells of transformed plants when coupled with a heterologous coding sequence in a chimeric gene. Further, the invention is directed to chimeric genes incorporating such promoter region, stable transfection of plants with these chimeric genes, and the plants and cells that are transfected, as well as seeds of such transfected plants. (page 4, line 32—page 5, line 3).

3. Timko et al. go on to describe the coding for PMT genes as their target.

Therefore, Timko et al. disclose conferring high levels of transcription of PMT (i.e. over expression of PMT) and as a result, higher levels of nicotine (page 5, 8-12).

4. Timko et al. compare low nicotine mutants with the engineered tobacco plants with transcripts encoding PMT, thus showing that increased nicotine tobacco plants were created:

Low alkaloid mutants of Burley 21 subjected to the same treatment show a much lower level of stimulation of *ODC* transcript accumulation after topping, and the enhanced transcript abundance does not persist beyond 4hr. By comparison, transcripts encoding PMT and a tobacco root-specific  $\beta$ -glucosidase (TBG-1) show patterns of accumulation similar to that observed for *ODC* transcripts in wild-type plants, but no induction in the low-alkaloid mutant, consistent with previous studies..." (page 29-30).

5. It would have been clear to one of ordinary skill in the art at the time of invention, that although Timko et al. do not explicitly state the phrase, "tobacco plants with increased nicotine", that the invention as detailed by Timko et al. would result in tobacco plants with increased levels of nicotine due to increased levels of PMT.

6. In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, Perkins et al. teach the use of tobacco and a source of additional nicotine to increase nicotine to the other smoke constituents in cigarette smoke. It would have been obvious to one of ordinary skill in the art, that the engineered tobacco of Timko et al. can be considered a tobacco with a source of additional nicotine, and would therefore be useful in the invention of Perkins et al.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

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the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 184 and 185 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (US 3,861,400) in view of Newton Jr. et al. (US 3,957,060), Timko (WO/00/67558), Russell (Nicotine and Public Health, 2000), and Gibson (US 3,878,850).

10. Perkins et al. disclose cigarettes with a tar to nicotine ratio between 3 and 8 (see Table I, examples 2, 4, and 6) and that the pH of the smoking material should be kept below approximately 6.5. However, Perkins et al. do not disclose that the tar to nicotine ratio was measured by FTC or ISO methods, the use of transgenic *Nicotiana tabacum* to supply nicotine, or that the pH of the cigarette smoke produced has a pH of 6.5 or lower.

11. Although Perkins et al. do not specifically disclose following FTC or ISO testing parameters however, the parameters disclosed are nearly identical to those of the FTC method as disclosed by the applicant. For instance, Perkins et al. disclose testing the cigarettes on a cigarette smoking machine with a 35 ml draw over 2 seconds every minute until 22 mm of cigarette are left. This compares to 35 ml draw over 2 seconds

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ever 58 seconds until 23 mm of cigarette are left. In both cases, the "Tar" equals the total particulate matter retained on a Cambridge filter with the weight of water and nicotine subtracted from the total particulate matter. It would have been obvious to one of ordinary skill in the art that the results obtained by Perkins et al. would not have been significantly different under FTC testing because the testing parameters are extremely similar. Furthermore, Perkins et al. teaches the general concept of increased tar to nicotine ratio, and it would have been obvious to one of ordinary skill in the art at the time of invention to manipulate the tar to nicotine ratio to produce a cigarette with low tar and medium nicotine. This is further suggested by the disclosure of Russell or the benefits that low tar medium nicotine cigarettes may present to habitual smokers (with tar to nicotine ratios of 9.9, 5.27, 8.61, 8.18 (i.e. the range encompasses from about 3 to about 8; see "Investigating the Low-Tar, Medium-Nicotine Approach").

12. Perkins et al. do not disclose the use of trasgenic *Nicotiana tabacum* in a cigarette. However, Timko et al. teach the engineering of *Nicotiana tabacum* to produce higher levels of nicotine using a heterologous coding sequence (nucleic acid encoding PMT) to boost levels of the putrescine N-methyltransferase (PMT) which is an enzyme whose presence is a rate limiting step in supplying a compound for nicotine synthesis in tobacco (page 4, 31-page 5, 5; page 3 paragraph 1) and thus increasing the production of nicotine. It would have been obvious to one of ordinary skill in the art at the time of invention to use the tobacco of Timko et al., which has higher levels of nicotine, in place of the added nicotine salts and compounds disclosed by Perkins et al. to produce a

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cigarette with the tar to nicotine ratios suggested by Perkins et al. and Russell. Doing so would have lead to predictable results (higher nicotine) and lower tar.

13. Although Perkins et al. describe the pH of the smoking material as being 6.5 or lower, Perkins et al. do not disclose the pH of the resulting cigarette smoke during use as being 6.5 or lower. However, the pH of tobacco smoke is generally considered to be acidic, and if the smoking material does not produce acidic smoke, it may present unwanted characteristics for smokers. For instance, Gibson et al. disclose that a “choky” flavor is associated with an alkaline trend in the pH of smoke and the “choky effect can diminished by making the smoke more acid (col. 1, 13-23). The examples of Gibson et al. illustrate several method of achieving lower pH smoke (lower than 6.5) with materials that may produce alkaline (basic) smoke. It would have been obvious to one of ordinary skill in the art at the time of invention to make the cigarette of Perkins et al. with the tobacco of Timko et al. and adjust the pH to lower than 6.5 by the methods and materials of Gibson et al. if the pH of the smoke produced was alkaline in nature or produced "choky" flavor.

14. Claim 186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perkins et al. (US 3,861,400), Newton Jr. et al. (US 3,957,060), Timko (WO/00/67558), Russell (Nicotine and Public Health, 2000), and Gibson (US 3,878,850) as applied to claim 184 above, in further view of Conkling et al. (US 6,423,520).

15. Timko et al. disclose using genetic engineering to increase expression or production of PMT, but do not disclose up-regulating quinolate phosphoribosyl

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transferase (QPT or QPRTase). However, Conkling et al. disclose creating a transgenic *Nicotiana* having increased QPRT expression when compared to altering the expression of QPRTase by using complimentary nucleic acid sequences encoding a segment of QPRTase (abstract). It would have been obvious to one of ordinary skill in the art at the time of invention to alter the expression of both QPRTase and PMT (PMTase) as these are the rate limiting enzymes for producing precursors for making nicotine as shown by Conkling et al. (figure 1). Conkling et al. indicate that QPRTase is a rate limiting enzyme in the production of nicotine and disclose increasing its expression or production (col. 1, 44-56), while Timko et al. disclose PMT as a rate limiting enzyme in the production of nicotine (see rejection of claim 184 above) and disclose increasing its expression or production. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the methods of Timko et al. and Conkling et al. to increase production of the two different, known, rate limiting enzymes in the production of Nicotine, and thus increasing nicotine production in transgeneic plants that result from the genetic manipulation.

### ***Conclusion***

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not



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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J. FELTON whose telephone number is (571)272-4805. The examiner can normally be reached on Monday to Friday, 7:30 AM to 4:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richard Crispino can be reached on 571-272-1226. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael J Felton/  
Examiner, Art Unit 1791

/Richard Crispino/  
Supervisory Patent Examiner, Art Unit 1747